

### **REMARKS**

Entry of the foregoing, reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested in light of the remarks which follow.

#### **I. Amendments to the Claims**

By the foregoing amendments to the claims, claims 12-29 and 39-46 have been amended, and new claims 53-55 have been added.

In particular, claim 12 has been amended to recite a fusion polypeptide comprising "SEQ ID NO: 2 fused in frame with a second polypeptide having cytosine deaminase activity." New dependent claim 53 recites that the fusion polypeptide is SEQ ID NO: 1. The claims have also been amended to recite "isolated" nucleic acids, vectors, host cells, and viral particles. In addition, the optional "substances" have been canceled from claim 14 and recited in new claim 54. Similarly, the specific viral vectors have been canceled from claim 17 and recited in new claim 55. The amendments to the claims are supported throughout the application as filed.

Additional amendments to the claims have also been made to clarify the claim language, for consistency, and to bring the claims into better conformance with U.S. patent practice. These amendments are merely editorial in nature and are not intended to change the scope of the claims or any elements recited therein.

The amendments to the claims have been made without prejudice or disclaimer to any subject matter recited or canceled herein. Applicants reserve the right to file one or more continuation and/or divisional applications directed to any canceled subject matter. No new matter has been added, and entry of the foregoing amendments to the above-identified application are respectfully requested.

#### **II. Response to Objections to the Drawings**

At page 3 of the Office Action, the Examiner has stated that the content in the square insert in Fig. 1 is unclear.

In response, Applicants submit herewith a corrected Fig. 1. Accordingly, Applicants respectfully request reconsideration and withdrawal of this objection.

**III. Response to Objections to the Specification**

At pages 3-4 of the Office Action, the Examiner has objected to the specification for a number of reasons.

In response, Applicants submit herewith a Substitute Specification. Accordingly, Applicants respectfully request reconsideration and withdrawal of this objection.

**IV. Response to Claim Rejections Under 35 U.S.C. § 101**

At pages 4-5 of the Office Action, claims 12-29 and 39-46 have been rejected under 35 U.S.C. § 101 for allegedly being directed to non-statutory subject matter.

In particular, the Examiner has indicated that because the rejected claims do not recite that the nucleic acid is "isolated," the claims are improperly directed to a product of nature.

In response, the claims have been amended to recite "isolated" nucleic acids, as recommended by the Examiner. Thus, Applicants respectfully request reconsideration and withdrawal of this rejection.

**V. Response to Claim Rejections Under 35 U.S.C. § 112, Second Paragraph**

At page 5 of the Office Action, claims 16 and 17 have been rejected under 35 U.S.C. § 112, second paragraph, as purportedly being indefinite.

In particular, the Examiner has stated that the term "derived from" is indefinite, because it is not clear how the viral vector that is "derived from" a virus may differ from the virus.

In response, the claims have been amended to recite that the viral vectors are "obtained from" a virus, as recommended by the Examiner. Thus, Applicants respectfully request reconsideration and withdrawal of this rejection.

**VI. Response to Claim Rejections Under 35 U.S.C. § 112, First Paragraph**

At pages 5-12 of the Office Action, claims 12-29 and 39-46 have been rejected under 35 U.S.C. § 112, first paragraph, as purportedly lacking enablement.

Specifically, the Examiner has stated that the specification does not disclose a representative number of sequences possessing the recited activity. Thus, the Examiner has concluded that specification does not enable the genus of polypeptides recited in the present claims. In addition, the Examiner has indicated that although Fcu1-8 is disclosed in the specification as an example of a polypeptide exhibiting CDase activity with loss of UPRTase

activity by changing Arg183 into Ser, the specification does not sufficiently identify the sequence of Fcu1. This rejection is respectfully traversed.

To expedite prosecution in the present application, and not to acquiesce to the Examiner's rejection, the claims have been amended as described above. In particular, the claims have been amended to recite fusion polypeptides comprising "SEQ ID NO: 2 fused in frame with a second polypeptide having cytosine deaminase activity." A dependent claim recites that the fusion polypeptide is SEQ ID NO: 1. Applicants respectfully submit that a person of ordinary skill in the art, at the time of filing, would have known how the Fcu1-8 variant relates to SEQ ID NOS: 1 and 2 in the present application.

Information which is known in the art need not be described in detail in the specification (*see, e.g. Hybritech, Inc v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 90 (Fed. Cir. 1986)). In addition, satisfaction of the written description requirement does not require either recitation or incorporation by reference of publicly accessible sequences (*see, e.g. Falkner v. Ingles*, 79 USPQ2d 1001 (Fed. Cir. 2006) and *Capon v. Eshhar*, 76 USPQ 1078 (Fed. Cir. 2005)).

The cases above support Applicant's position that the present application sufficiently describes the sequences Fcu1 and Fcu1-8. In particular, a person of ordinary skill in the art would have recognized that the sequence of the polypeptide Fcu1-8 is the same as that of Fcu1, except that the Arg residue at position 183 of Fcu1 has been substituted with Ser (*see* Example 1). Furthermore, the sequence of Fcu1 was known in the art at the time of filing, and is described, for example, in SEQ ID NO: 2 of WO99/54481, cited in the present specification at page 4, lines 13-15 (*see, also, Erbs et al.*, Cancer Res. 60:3813-3822 (2000)). Given the public availability of the Fcu1 sequence, a person of ordinary skill in the art would have readily arrived at the sequence of Fcu1-8, simply by substituting the relevant Arg residue for Ser.

In addition, SEQ ID NO: 1 in the present application corresponds to Fcu1-8. Because SEQ ID NO: 1 in the present application differs from SEQ ID NO: 2 in the '481 publication in that the Arg residue at position 183 has been substituted with Ser, a person of ordinary skill in the art would have immediately recognized that the present SEQ ID NO: 1 is the Fcu1-8 sequence.

Furthermore, the portion of Fcu1-8 that is obtained from the Fur1 polypeptide clearly corresponds to SEQ ID NO: 2 in the present application. In particular, the present application describes a polypeptide Fur1 whose first 35 N-terminal residues have been

deleted, *i.e.* FUR1 $\Delta$ 105 (the fusion of FUR1 $\Delta$ 105 and FCY1 yields FCU1; *see, e.g.*, Example 5 of WO 99/54481 and Erbs et al., Fig. 1). SEQ ID NO: 1 of WO 99/54481 comprises the amino acid sequence of FUR1 $\Delta$ 105 comprising in addition the substitution of the Ser residue at position 2 with an Ala residue. A person of ordinary skill in the art would readily recognize that SEQ ID NO: 1 of the '481 publication differs from SEQ ID NO: 2 of the present application in that the Arg residue at position 26 of SEQ ID NO: 1 has been substituted with a Ser residue in SEQ ID NO: 2; and that the additional substitution of the Ser residue at position 2 with an Ala residue contained in SEQ ID NO: 1 is not present in SEQ ID NO: 2. Therefore, a person of ordinary skill would have known that present SEQ ID NO: 2 corresponds to FUR1 $\Delta$ 105 wherein the Arg residue at position 26 has been substituted with a Ser residue. Thus, the person of ordinary skill in the art, at the time of filing, would have known how Fcu1 and Fcu1-8 relate to SEQ ID NO: 2 in the present application.

Finally, the sequences of a representative number of "polypeptides having cytosine deaminase activity," suitable for use in the present fusion proteins, are described in the specification and/or were publicly available at the time of filing.

Accordingly, the present claims are fully enabled, and Applicants respectfully request reconsideration and withdrawal of this rejection.

**CONCLUSION**

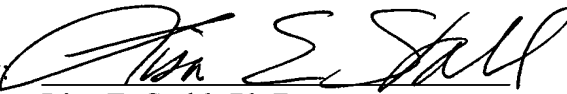
From the foregoing, further and favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully requested to telephone the undersigned so that prosecution of the application may be expedited.

Respectfully submitted,

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